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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/654,462	09/01/2000	Thomas M. Jessell	62166.JPW.EMW	6093

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EXAMINER	
FALK, ANNE MARIE	

ART UNIT	PAPER NUMBER
1632	18

DATE MAILED: 12/04/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Application No.	Applicant(s)
09/654,462	JESSELL ET AL
Examiner	**Art Unit**
Anne-Marie Falk, Ph.D.	1632

Office Action Summary

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) *5-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8 and 12* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The response filed September 18, 2002 (Paper No. 17) has been entered.

Claims 1-12 are pending in the instant application.

Applicants' election with traverse of Group I, Claims 1-4 in Paper No. 17 is acknowledged. The traversal is on the grounds that there would not be a serious burden in performing a search and examination of both inventions because a search of prior art for the invention of Group I, drawn to a method of converting a stem cell into a ventral neuron using the nucleic acid of homeodomain transcription factor Nkx6.1 will reveal whether any prior art exists for a method of diagnosing a motor neuron degenerative disease. However, this is not found persuasive because a search for the invention of Group I would not be considered a comprehensive search for the method of the invention of Group II, which is directed to distinct subject matter in that it involves diagnosing a motor neuron degenerative disease. Prior art that would be used in a rejection of the invention of Group I would not be used in a rejection of the invention of Group II, because the methods are not obvious over each other. The methods are patentably distinct and a search for the method of Group I would not identify art relevant to Group II. Therefore, additional searching would be required to cover the invention of Group II. Because the searches are not coextensive, a search and examination of both inventions in a single patent application would constitute a serious burden on the Examiner.

The requirement is still deemed proper and is therefore made FINAL.

The elected invention is drawn to a method of converting a stem cell into a ventral neuron.

Claims 5-12 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention. Election was made with traverse in Paper No. 17.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are directed to a method of converting a stem cell to a ventral neuron. The claims cover *in vivo* and *in vitro* applications of the claimed method.

The specification fails to provide an enabling disclosure for the claimed method because the specification does not offer specific guidance with regard to the type of stem cell that can be used to produce a ventral neuron using the method as claimed. The claims cover the use of any type of stem cell to produce a ventral neuron upon introducing a nucleic acid encoding the Nkx6.1 homeodomain transcription factor. However, the specification does not offer any guidance with regard to which type of stem cells could be used to produce a ventral neuron, nor does it provide culture conditions that would be suitable for inducing a stem cell to differentiate into a ventral neuron. For example, there is no teaching in the specification for using a hematopoietic stem cell in the claimed method. There is no teaching of specific culture conditions that would permit a hematopoietic stem cell to differentiate into a ventral neuron. The state of the art is such that methods of provoking a particular type of stem cell to differentiate into a particular type of differentiated cell are not developed by routine experimentation. Furthermore, different types of stem cells have differing potentialities in terms of the types of cells they are capable of differentiating into (see pp. 1-9 of Stem Cells: Scientific Progress and Future Research Directions, June 2001).

The specification fails to provide an enabling disclosure for *in vivo* applications of the claimed method because the specification does not provide specific guidance for practicing the claimed invention *in vivo*. Furthermore, the specification does not assert a utility for practicing the claimed method *in vivo* and the only potential utility for producing neurons *in vivo* is for therapy. If practiced *in vivo*, the claimed method encompasses gene therapy. However, the specification fails to provide an enabling disclosure for the claimed method because the specification does not enable gene therapy. The specification does not teach how to use the claimed methods in gene therapy applications, for the following reasons.

The claims involve the introduction of a nucleic acid encoding a transcription factor protein into a stem cell. Thus, the claims are clearly cover methods of gene therapy. However, gene therapy is not routinely successful. Therefore, the disclosure must enable the full scope of the claimed methods with specific guidance. However, the specification fails to teach any method for introducing a nucleic acid encoding the Nkx6.1 transcription factor into a stem cell residing *in vivo* and expressing that gene at a level sufficient to produce ventral neurons and thereby achieve a therapeutic effect in a diseased immunocompetent animal. The specification does not provide any guidance as to the level of gene expression required, the type of gene transfer vector to be used, the number of transduced cells needed, the route and time course of administration, when, where, or for how long the therapeutic gene should be expressed, the frequency of administration of the gene therapy vector, or the intended target tissue, for treatment of any pathological condition in an immunocompetent animal. The specification also lacks any working examples showing that the contemplated nucleic acid, once delivered to the appropriate site, would be expressed at a level sufficient to provide adequate product to effect a therapeutic result in an immunocompetent animal. At the time the application was filed, the art of administering any type of genetic expression vector to an individual so as to provide a tangible therapeutic benefit was poorly developed and unpredictable. The NIH ad hoc committee to assess the current status and promise of gene therapy reported in December 1995 that "clinical efficacy has not been definitively demonstrated at this

time in any gene therapy protocol, despite anecdotal claims...," and that "significant problems remain in all basic aspects of gene therapy" (Orkin and Motulsky, p. 1). In a review article published in Scientific American in June 1997, Theodore Friedmann discusses the technical barriers which have so far prevented successful gene therapy, and states "So far, however, no approach has definitively improved the health of a single one of the more than 2,000 patients who have enrolled in gene therapy trials worldwide" (p. 96). In a review article published in Nature in September 1997, Inder Verma states "Although more than 200 clinical trials are currently underway worldwide, with hundreds of patients enrolled, there is still no single outcome that we can point to as a success story" (p. 239). The instant specification does not adequately teach one skilled in the art how to use the claimed methods for *in vivo* gene therapy. Moreover, the instant specification does not assert any other use for practicing the claimed method *in vivo*. Thus, absent any showing that the claimed methods can be used in gene therapy applications to produce a therapeutic effect in an immunocompetent animal, such as a human, claims covering gene therapy are not enabled by the disclosure.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne-Marie Falk whose telephone number is (703) 306-9155. The examiner can normally be reached Monday through Thursday and alternate Fridays from 10:00 AM to 7:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the patent analyst, Tiffiany Tabb, whose telephone number is (703) 305-1238.

Anne-Marie Falk, Ph.D.

Anne-Marie Falk
ANNE-MARIE BAKER
PATENT EXAMINER